Profenofos Technical Briefing

June 16, 1999

Introduction and Background Information

Introduction

Purpose of Briefing

- Present overview of profenofos risk estimates.
- Begin next phase of public participation (TRAC Pilot Process).
- Identify where to focus mitigation.

Introduction (*continued*)

Profenofos Risk Assessments Consider:

- **Dietary Risk**: *food, drinking water, and aggregate*
- **Worker Risk**: *applicators, handlers, and postapplication workers*
- **Ecological Risks**: *birds, mammals, fish, and other aquatic species*

Profenofos Risk Assessments *DO NOT* Consider:

- **Residential Risk:** *Profenofos has no residential or public health uses.*

Introduction (*continued*)

TRAC Pilot Public Participation Process for Profenofos

Phase	Health Effects Assessment	Ecological Assessment
❶ "Error Only" Review	N/A	N/A
❷ Public Docket Opened	8/98	8/98
❸ Comment Period Completed	10/98	10/98
❹ Revised Assessment to USDA	2/99	2/99
❺ Solicit Risk Mgt. Options	6/16/99	6/16/99
❻ Develop Risk Mgt. Strategy		

Introduction *(continued)*

Phase 1: "Error Only" Review

Phase 2: Open Public Docket

- 60-day public comment period.

Introduction *(continued)*

Phase 3: Public Participation

- Comments received from registrant, public interest groups, growers, USDA
  - Importance to agriculture
  - Used in IPM programs
  - Alternatives
- New Information Identified:
  - Information on ecological risks (fish)

Introduction *(continued)*

Phase 4: Revise Assessments, Solicit Comments from USDA

- **Revisions to dietary assessment:**
  - DEEM™ program and USDA food consumption database
  - Updated percent of crop treated
- **Clarified worker risk assessment:**
  - Added exposure estimates for various reentry intervals
  - Clarified methodology and supporting studies

Introduction *(continued)*

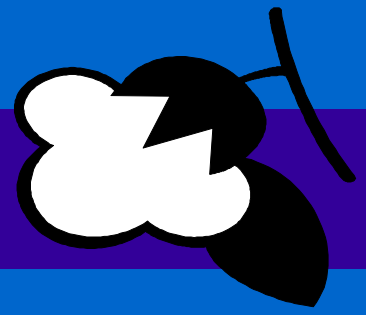
Phase 4: Revise Assessments, Solicit Comments from USDA (con't)

- **Modifications to ecological assessment**
  - Re-characterized potential environmental effects on aquatic animals.
- **Comments from USDA on human health and ecological effects assessment.**

Regulatory History

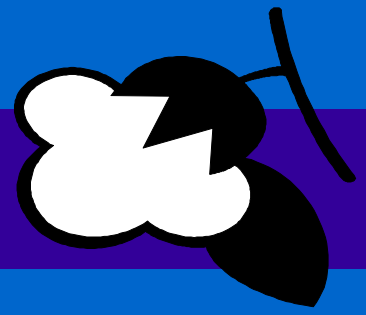
- No Registration Standard issued.
- Tolerances established.
- Voluntary measures by registrant to address fish kills.

Use Profile



- Profenofos is an insecticide/miticide.
- It was first registered by Ciba-Geigy, in 1982
- Currently registered by Novartis
- Registered Uses: Cotton only
  - restricted use pesticide
  - Food Uses:
    - *cottonseed oil,*
    - *milk, and*
    - *meat byproducts*

Use Profile (*continued*)



Profenofos Controls:

- mites
- whiteflies
- aphids
- cotton leafperforator
- tobacco budworm
- cotton bollworm
- beet armyworm
- fall armyworm

Use Profile (*continued*)

Use Practices

- Sprayed on cotton aerially and via groundboom.
- Typical application rates are:
  - Early season: 0.125 to 0.5 lb ai/A
  - Mid to late season: 0.25 to 1.0 lb ai/A
- Maximum of 6 applications per season are allowed
  - Average is ~2
- Reentry Interval -- 48 or 72 hours

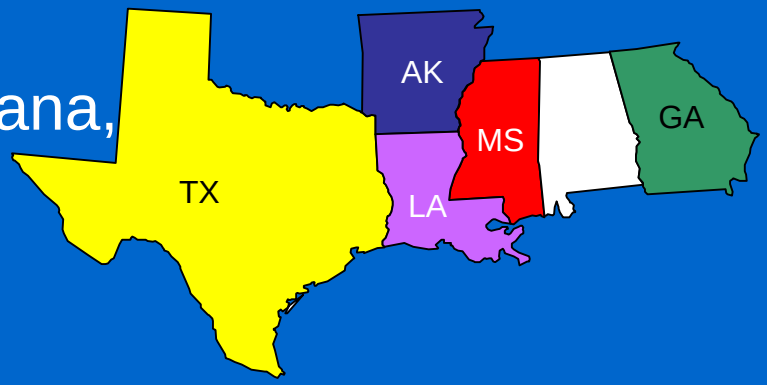
Use Profile (*continued*)

Usage

- 775,000 pounds used per year (*weighted average*)
- 5-10% Crop Treated (CT)

Major Use Regions

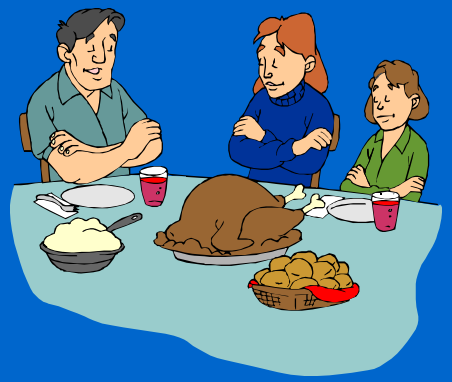
- Mississippi, Texas, Louisiana, Georgia, and Arkansas



Sources of Use Data

- USDA/NASS
- California Department of Pesticide Regulation
- Other Sources (e.g., growers and registrant)

Human Health Risk Assessment



Risk Assessment Components

Risk Assessment Components:

- Dietary:
  - Food
  - Drinking Water
- Occupational
  - Application
  - Postapplication

***NOTE*:** *There are no residential uses of profenofos*

Basic Risk Equation

Risk = Hazard x Exposure, where

Exposure = Consumption x Residue

Analysis of Special Sensitivity for Infants and Children

FQPA 10X Safety Factor Removed:

- No developmental effects in fetuses below maternally toxic doses.
- No increased sensitivity in pups relative to adults.
- No abnormalities in developing fetal nervous system.
- No neuropathology.
- Complete toxicity database.

Dietary Risk Assessments

Acute

- *estimate of the range of exposures that individuals could encounter on a single day.*

Chronic

- *estimate of a person's average dietary exposure over the long-term (e.g., several years to a lifetime).*

Acute Risk Assessment

Acute Risk (% aPAD) =

$$\frac{\text{Maximum Exposure (mg/kg/day)}}{\text{Acute Population Adjusted Dose (aPAD)}} x100$$

where,

$$\text{aPAD} = \frac{\text{acute Reference Dose}}{\text{FQPA Safety Factor}}$$

Acute Hazard (toxicity)

Study:	Rat Oral Acute Neurotoxicity
Endpoint:	Plasma/Red Blood Cell Cholinesterase Inhibition
NOAEL:	0.5 mg/kg/day
LOAEL:	25 mg/kg/day

Acute Population Adjusted Dose (aPAD)

aPAD = 0.005 mg/kg/day, based on:

- NOAEL of 0.5 mg/kg/day
- Uncertainty Factors:
  - 10X interspecies extrapolation
  - 10X intraspecies variability
  - 1X FQPA Safety Factor

Acute Exposure Estimates

Based on:

- 10% CT (estimated maximum);
- Anticipated residues in cottonseed oil/milk/meat;
  - 1/2 LOQ assumed.
- Food Consumption data from USDA Continuing Survey of Food Intake by Individuals (CSFII) 1989-91, and;
- DEEM Software

Acute Risk Estimates

Population	% aPAD at the 95th Percentile[1]
General U.S	4
Infants<1 yr.	8
Children 1-6	8
Children 7-12	5

[1]***NOTE.*** *Non-probabilistic: Risk at 95th percentile of exposure.*

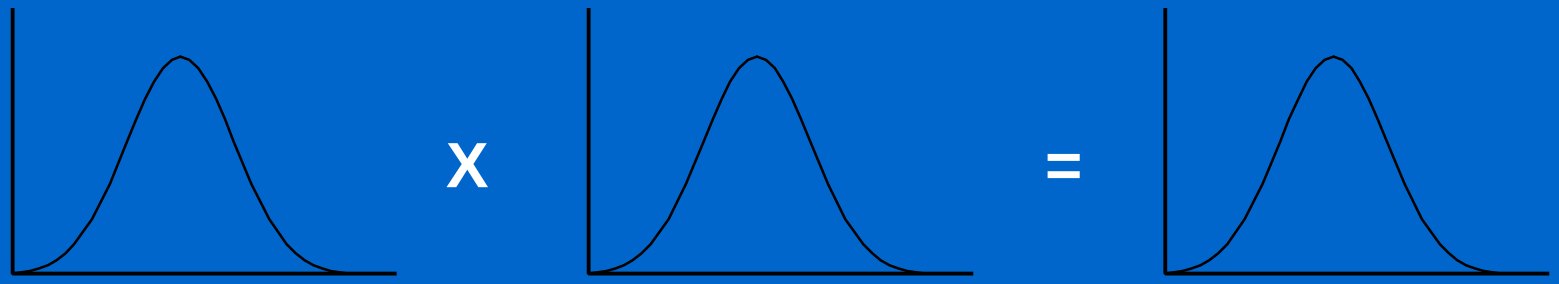
Two Types of Acute Dietary Risk Assessments

Non-Probabilistic

Assumes that every piece of fruit or vegetable consumed has residues at a high level. Therefore, a consumer's chance of consuming a high-residue piece of fruit or vegetable depends entirely on whether he or she eats that fruit or vegetable.

Two Types of Acute Dietary Risk Assessments *(cont.)*

Probabilistic



All Consumption Values | All Residue Values | Range of Dietary Exposures

Assumes that any one piece of fruit or vegetable consumed can have residues anywhere in the range of residues observed. Therefore, a consumer's chance of consuming a high-residue piece of fruit or vegetable depends both on how much of the item he or she eats AND how frequently that item is found to have high residues.

More realistic exposure estimates.

Chronic Risk Assessment

Chronic Risk (% cPAD) =

$$\frac{\text{Average Exposure (mg/kg/day)}}{\text{Chronic Population Adjusted Dose (cPAD)}} x100$$

where,

$$\text{cPAD} = \frac{\text{chronic Reference Dose}}{\text{FQPA Safety Factor}}$$

Chronic Hazard (toxicity)

Study:	Six-Month Oral Dog
Endpoint:	Plasma/Red Blood Cell Cholinesterase Inhibition
NOAEL:	0.005 mg/kg/day
LOAEL:	0.05 mg/kg/day

Chronic Population Adjusted Dose (cPAD)

cPAD = 0.00005 mg/kg/day, based on:

- NOAEL of 0.005 mg/kg/day
- **Uncertainty Factors:**
  - 10X interspecies extrapolation
  - 10X intraspecies variability
  - 1X FQPA Safety Factor

Chronic Exposure Estimates

Based on:

- 5% CT (weighted average);
- Food Consumption data from USDA Continuing Survey of Food Intake by Individuals (CSFII) 1989-91;
- DEEM Software; and
- Anticipated Residues (processing study for cottonseed oil and feeding studies in livestock)
  - 1/2 LOQ used.

***NOTE**: All residue estimates are less than the level of quantitation.*

Chronic Risk Estimates

Population	% cPAD
General U.S	6
Infants<1 yr.	10
Children 1-6	18
Children 7-12	11

Drinking Water Exposure

- **Estimates Are Based on**:
  - Agency default consumption values of:
    - 2 liters/day for adults; and
    - 1 liter/day for children.
  - Upper-end surface water contamination values from screening-level mathematical models (*peak and annualized*)

Drinking Water Risk Estimates

- **Methodology**:
  - Determined exposure to profenofos in food, then considered exposure in drinking water and compared the total to acute and chronic PAD.
- **Acute Risk** (*based on model estimate*) is:
  - 92% of the acute PAD remaining after acute food exposure is considered.
- **Chronic Risk** (*based on model estimate*) is:
  - 82% of the chronic PAD remaining after chronic food exposure is considered.

Drinking Water Risk Conclusions

- **Acute and Chronic Risk**:
  - When the exposure due to ingesting profenofos-contaminated drinking water is added to the food source exposure, both for acute and chronic risk estimates, 100% of the aPAD and cPAD, respectively, is not exceeded.
- **Conclusion:**
  - There is a reasonable certainty that no harm will result to infants, children, or any population subgroup from acute and/or chronic exposure to drinking water contaminated with profenofos.

Aggregate Risk Assessment

- Includes exposures from various sources:
  - food, drinking water, and residential and other non-occupational.
- No registered residential uses:
  - For example, profenofos is not registered for use in homes, on lawns, golf courses, etc.
- Aggregate risk assessment for profenofos includes food and drinking water only.

Aggregate Risk Assessment (con't)

For Profenofos, Aggregate Risk Estimates Are:

Less than the acute and chronic PAD for all population subgroups including infants and children.

Occupational Risk Assessments for Profenofos

Handlers

- *includes professional pesticide applicators and farmer/growers who mix, load and apply pesticides.*

Postapplication Workers

- *includes workers who prune, thin, hoe, prop, and harvest crops following pesticide application.*

Handler Assessment

Factors Forming the Basis for Risk Assessment

- Formulation and application equipment (e.g., emulsifiable liquid, groundboom, aerial)
- Unit exposure (mg ai/lb ai handled)
- Rate of application (lb ai/acre)
- Areas treated per day (e.g., acres/day)
- Levels of protection
- Toxicity endpoint (mg/kg/day)

Toxicity Endpoints for Occupational Risk Assessment

Short- and Intermediate Term for Dermal and Inhalation Exposure

Dermal	**Study**	21-day dermal toxicity in rabbits
	NOAEL	1mg/kg/day
Inhalation	**Study**	21-day inhalation in rats
	LOAEL	0.068 mg/L (9.7 mg/kg/day)
Endpoint:		decreases in cholinesterase activities in red blood cells, serum, and the brain

Handler Assessment (*continued*)

Handler Risk Calculations (dermal)

$$MOE = \frac{NOAEL\ (mg/kg/day)}{Dose\ (mg/kg/day)}$$

where,

$$Dose = \frac{(unit\ exposure) \times (appl.\ rate) \times (acres/day) \times (\%dermal\ absorption)}{Body\ Weight}$$

NOTE: *Correction for dermal absorption is not required for short- and intermediate-term risk assessment (21-day dermal study).*

Handler Assessment (*continued*)

- **Data Sources:**
  - Labels
  - Use Information
  - Standard Assumptions
  - Chemical-Specific Studies
  - Pesticide Handlers Exposure Database (PHED)

Pesticide Handlers Exposure Database (PHED)

- Developed by Task Force of:
  - USEPA;
  - Health Canada;
  - California DPR; and
  - ACPA
- Contains actual monitored data generated by registrants.
- Harmonized use of the database.

PHED Strengths

- Most complete source of pesticide monitoring data available.
- Data and system extensively peer reviewed.
- Adds consistency to risk assessments.
- Widely accepted by industry and others.

Handler Assessment Scenarios

- **Mixing/Loading Liquids:**
  - Groundboom, or
  - Aerial Applications.
- **Applying Liquids:**
  - Groundboom, or
  - Aerial Applications.
- **Flagging:**
  - Aerial Applications

Handler Assessment - *Short/Intermediate Term*

Groundboom Application *(combined dermal and inhalation; 80 acres treated)*

Activity	MOE with PPE[1]	MOE with Engineering Controls[2]
Mixing/Loading (M/L)	50	101
Applying (A)	83	172

[1]Double layer of clothing, chemical-resistant gloves (M/L,A)

[2]Closed system, single layer clothing, chemical-resistant gloves (M/L); and Enclosed cab, single layer clothing (A)

Handler Assessment - *Short/Intermediate Term*

Aerial Application *(combined dermal and inhalation; 350 acres treated)*

Activity	MOE with PPE[1]	MOE with Engineering Controls[2]
Mixing/Loading (M/L)	12	23
Applying (A)	-	40
Flagging (F)	20	1000

[1]Double layer of clothing, chemical-resistant gloves (M/L); Double layer of clothing (F)

[2]Closed system, single layer clothing, chemical-resistant gloves (M/L); Enclosed cockpit, single layer clothing (Pilot); Enclosed cab, single layer clothing (F)

Handler Assessment *(continued)*

Discussion of Results for Short- and Intermediate-Term Risks:

- Groundboom application scenarios had MOE's *above* 100 with engineering controls
- Aerial application scenarios had MOE's *below* 100 with engineering controls,
  - except, for flaggers, whose MOE was well *above* 100.

Postapplication Worker Assessment

Factors Forming Basis for Risk Assessment

- Dislodgeable Foliar Residue (DFR):
  - *amount of residue that workers could contact in field.*
- Transfer Coefficient (Tc):
  - *indicator of amount that worker actually contacts during various activities.*

Postapplication Worker Assessment (*continued*)

Postapplication Worker Risk Calculations

$$MOE = \frac{NOAEL\ (mg/kg/day)}{Dose\ (mg/kg/day)}$$

where,

$$Dose = \frac{DFR\ (\mu g/cm2) \times Tc\ (cm2/hour) \times 8\ hours}{Body\ Weight\ (kg)}$$

Postapplication Worker Assessment (*continued*)

Sources of Information

- **DFR Data:**
  - Registrant conducted studies in four states (CA,TX, SC, NC)
- **Transfer Coefficients:**
  - Derived from registrant conducted exposure studies on hoers and scouts in two states (NC,SC)

Postapplication Worker Assessment (*continued*)

Risk Assessment Results

Activity	Days after Treatment	MOE
Hoeing	4	110
Scouting	8	108

Profenofos Incidents

- **Incident Data System:**
  - 7 allegations of minor affects from application and spray drift
- **Poison Control Centers 1985-96:**
  - 5 occupational cases; and
  - 10 non-occupational due to profenofos alone (e.g., spray drift)
- **California 1982-1993:**
  - 2 handler systemic poisonings, and
  - 4 fieldworker cases with skin or eye irritation only

Profenofos Incidents (*continued*)

- Very few reports of adverse effects in humans and domestic animals.
- Ratio of poisoning to applications low compared to other OP's

Ecological Assessment

Environmental Fate And Effects Assessment

- **Environmental Fate Assessment:**
  - *Lab and Field Studies*
- **Water Resource Assessment:**
  - *Monitoring and Modeling*
- **Ecological Toxicity:**
  - *Acute and Chronic Risks*
- **Ecological Risk Assessment:**
  - *Exposure and Toxicity, Incidents*

Environmental Fate of Profenofos

- **Major Route of Degradation**:
  - pH-dependent hydrolysis
- **Soil Degradation:**
  - Degrades rapidly in alkaline soils; likely more persistent in acidic to neutral soils
- **Mobility:**
  - Not highly mobile; may reach surface waters but is not expected to leach to groundwater under normal use.

Drinking Water and Aquatic Assessment of Profenofos

- Expect profenofos to reach surface water but not groundwater.
- Persistence in surface water pH-dependent.
- Little monitoring data are available.
- Relied on modeling to estimate aquatic exposure.

Summary of Ecological Toxicity

Species	Toxicity
Birds	Moderately to Highly Toxic
Small Mammals	Moderately Toxic
Bees	Highly Toxic
Fish and Aquatic Invertebrates	Highly to Very Highly Toxic

Ecological Risk Assessment: *Toxicity + Exposure*

- **Risk Quotients (RQ):** *Ratio of exposure concentration to toxicity endpoint*

$$\text{Acute RQ} = \frac{\text{Peak environmental concentration}}{\text{LD50, LC50, or EC50}}$$

$$\text{Chronic RQ} = \frac{\text{Long-term average concentration}}{\text{NOAEC or LOAEC}}$$

- Ratio is compared to Levels of Concern (LOC)

Summary Of Ecological Risk Assessment: *Aquatic*

Risk to Fish and Aquatic Invertebrates

Duration	RQ's	
	Level of Concern	Actual
Acute	≥0.5	<0.1 to 6.4
Chronic	≥1 (*for survival*)	5.2 to 5.8

Summary Of Ecological Risk Assessment: *Terrestrial*

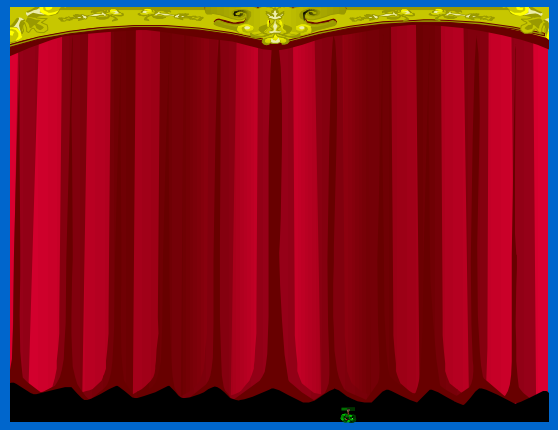
Risk to Birds and Small Mammals

Species and Duration		RQ's	
		Level of Concern	Actual
Acute	Avian	RQs ≥ 0.5	0.2 to 4.2
	Small Mammal		0.1 to 0.8
Chronic Avian		RQs ≥ 1	as high as 24 (for egg production)

Incidents Confirm Acute Aquatic Risk

- **13 fish kill incidents in LA, MS, 1994 - 1996**
  - Residues in fish, water verify presence of profenofos
  - Probable result of maximum label use during budworm outbreak (USDA)
- **Conditions favoring potential fish kills from profenofos use**
  - regions with neutral to acidic soil and water, prone to runoff
  - high application rate
  - heavy rainfalls shortly after application

Summary and Conclusion



In Summary….

- The TRAC Pilot Process helped to improve explanations of risk.
- There's little dietary risk posed by the use of profenofos on cotton.
- Areas of concern remaining are:
  - Handler and postapplication risk
  - Risk to non-target aquatic species (especially fish)